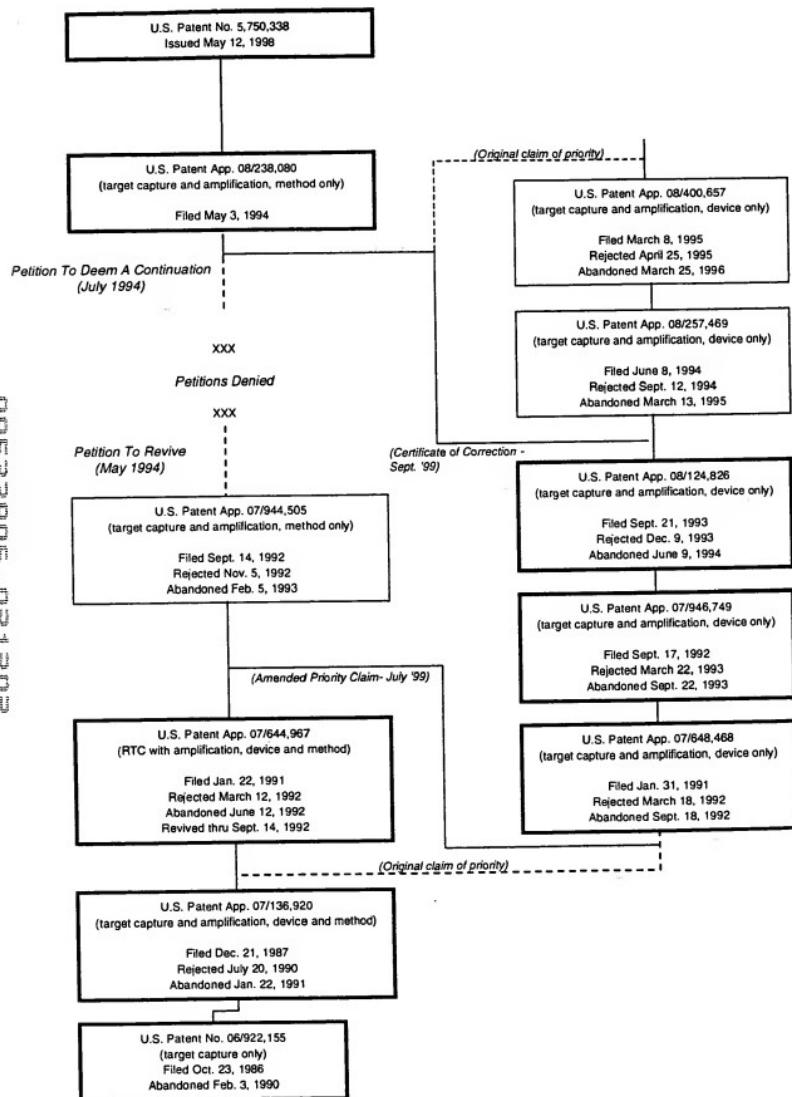


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'338 PATENT HISTORY WITH POST-ISSUANCE CORRECTIONS AND AMENDMENTS



1 STEPHEN P. SWINTON (106398)
2 J. CHRISTOPHER JACZKO (149317)
COOLEY GODWARD LLP
3 4365 Executive Drive, Suite 1100
San Diego, California 92121-2128
4 Telephone: (858) 550-6000
Facsimile: (858) 453-3555

5 DOUGLAS E. OLSON (38649)
6 BROBECK, PHLEGER & HARRISON LLP
12390 El Camino Real
7 San Diego, California 92130-2081
Telephone: (858) 720-2500
8 Facsimile: (858) 720-2555

9 R. WILLIAM BOWEN, JR. (102178)
GEN-PROBE INCORPORATED
10 10210 Genetic Center Drive
San Diego, California 92121-4362
11 Telephone: (858) 410-8918
Facsimile: (858) 410-8637

12 Attorneys for Plaintiff
13 Gen-Probe Incorporated

14 UNITED STATES DISTRICT COURT
15 SOUTHERN DISTRICT OF CALIFORNIA

16 GEN-PROBE INCORPORATED,
17 Plaintiff,
18 v.
19 VYSIS, INC.,
20 Defendant.

No. 99-CV-2668H AJB
JUDGE MARILYN L. HUFF

REPLY DECLARATION OF STEPHEN P.
SWINTON IN SUPPORT OF GEN-PROBE'S
MOTION FOR PARTIAL SUMMARY JUDGMENT

Date: June 8, 2001
Time: 10:30 a.m.
Dept: Courtroom 1

21 I, Stephen P. Swinton, declare as follows:

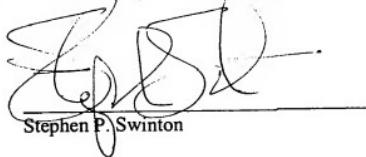
22 1. I am a member of the State Bar of California and admitted to practice before this
23 Court. I am a partner with the law firm of Cooley Godward LLP and am one of the counsel of

1 record in this action for plaintiff Gen-Probe Incorporated.

2 2. I attended the deposition of Walter King, Ph.D., at Downers Grove, Illinois on
3 April 18, 2001. I asked the questions and heard the responses given by Dr. Lawrie at the
4 deposition. The deposition of Dr. King was stenographically recorded and transcribed. The
5 excerpts of the Lawrie deposition set forth in Exhibit 17 to the accompanying Reply Notice of
6 Lodgment are true and correct copies of the certified deposition transcript and accurately state the
7 questions and answers at the King deposition.

8 3. I attended the deposition of Donald Neil Halbert, at Abbot, Illinois on April 19,
9 2001. I asked the questions and heard the responses given by Dr. Halbert at the deposition. The
10 deposition of Dr. Halbert was stenographically recorded and transcribed. The excerpts of the
11 Halbert deposition set forth in Exhibit 18 to the accompanying Reply Notice of Lodgment are true
12 and correct copies of the certified deposition transcript and accurately state the questions and
13 answers at the Halbert deposition.

14 I declare under penalty of perjury under the laws of the United States of America that all
15 statements made herein of my own knowledge are true and that all statements made on information
16 and belief are believed to be true. This declaration was executed by me at San Diego, California
17 on May 31, 2001.


Stephen P. Swinton

1 STEPHEN P. SWINTON (106398)
2 J. CHRISTOPHER JACZKO (149317)
3 COOLEY GODWARD LLP
4 4365 Executive Drive, Suite 1100
5 San Diego, CA 92121-2128
6 Telephone: (858) 550-6000
7 Facsimile: (858) 453-3555

8 DOUGLAS E. OLSON (38649)
9 BROBECK PHLEGGER & HARRISON LLP
10 12390 El Camino Real
11 San Diego, CA 92130
Telephone: (858) 720-2500
Facsimile: (858) 720-2555

R. WILLIAM BOWEN, JR. (102178)
GEN-PROBE INCORPORATED
10210 Genetic Center Drive
San Diego, CA 92121-4362
Telephone: (858) 410-8918
Facsimile: (858) 410-8637

Attorneys for Plaintiff
GEN-PROBE INCORPORATED

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF CALIFORNIA

GEN-PROBE INCORPORATED,

No. 99CV2668 H (AJB)
THE HONORABLE MARILYN L. HUFF

Plaintiff,

REPLY DECLARATION OF R. WILLIAM BOWEN
IN SUPPORT OF GEN-PROBE'S MOTION FOR
SUMMARY JUDGMENT

v.

VYSIS, INC.,

Defendant.

Date: June 8, 2001
Time: 10:30 a.m.
Place: Courtroom 1

I, R. William Bowen, declare as follows:

1. I am a member of the State Bar of California and admitted to practice before this Court. I am one of the counsel of record in this action for plaintiff Gen-Probe Incorporated.
2. I attended the deposition of Anthony J. Janiuk, Esq. at Boston, Massachusetts on May 16, 2001. I asked the questions and heard the responses given by Mr. Janiuk at the deposition. The deposition of Mr. Janiuk was stenographically recorded and transcribed. The

1 excerpts of the Janiuk deposition set forth in Exhibit 13 to the accompanying reply notice of
2 lodgment are true and correct copies of the certified deposition transcript and accurately state the
3 questions and answers at the Janiuk deposition.

4 3. At the deposition of Mr. Janiuk, a letter dated November 14, 1989 from Mr. Janiuk
5 to Dr. James Richards was marked as Plaintiff's Deposition Exhibit 143 and authenticated by the
6 witness. A true and correct copy of this letter is attached as Exhibit 11 to the accompanying reply
7 notice of lodgment.

8 4. I attended the deposition of Alan E. Smith, Ph.D., at Cambridge, Massachusetts on
9 May 17, 2001. I asked the questions and heard the responses given by Dr. Smith at the deposition.
10 The deposition of Dr. Smith was stenographically recorded and transcribed. The excerpts of the
11 Smith deposition set forth in Exhibit 14 to the accompanying reply notice of lodgment are true and
12 correct copies of the certified deposition transcript and accurately state the questions and answers
13 at the Smith deposition.

14 5. I attended the deposition of David Ward, Ph.D., at New Haven, Connecticut on
15 May 18, 2001. I asked the questions and heard the responses given by Dr. Ward at the deposition.
16 The deposition of Dr. Ward was stenographically recorded and transcribed. The excerpts of the
17 Ward deposition set forth in Exhibit 15 to the accompanying reply notice of lodgment are true and
18 correct copies from the preliminary or "rough" deposition transcript and accurately state the
19 questions and answers at the Ward deposition.

20 6. I attended the deposition of Jon Lawrie, Ph.D., at Raleigh - Durham, North Carolina
21 on February 15, 2001. I asked the questions and heard the responses given by Dr. Lawrie at the
22 deposition. The deposition of Dr. Lawrie was stenographically recorded and transcribed. The
23 excerpts of the Lawrie deposition set forth in Exhibit 16 to the accompanying reply notice of
24 lodgment are true and correct copies of the certified deposition transcript and accurately state the
25 questions and answers at the Lawrie deposition.

26 7. At the deposition of Dr. Lawrie, a set of handwritten notes made by Dr. Lawrie was
27 marked as Plaintiff's Deposition Exhibit 49 and authenticated by the witness. A true and correct
28 copy of page these notes is attached as Exhibit 12 to the accompanying reply notice of lodgment.

1 I hereby declare under penalty of perjury that all statements made herein of my own
2 knowledge are true and that all statements made on information and belief are believed to be true.
3 Executed at San Diego, California on May 31, 2001.

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5 R. William Bowen
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R. William Bowen

1 COOLEY GODWARD LLP
2 STEPHEN P. SWINTON (106398)
3 J. CHRISTOPHER JACZKO (149317)
4 4365 Executive Drive, Suite 1100
5 San Diego, California 92121-2128
6 Telephone: (858) 550-6000
7 Facsimile: (858) 453-3555

8 DOUGLAS E. OLSON (38649)
9 BROBECK, PHLEGER & HARRISON LLP
10 12390 El Camino Real
11 San Diego, California 92130-2081
12 Telephone: (858) 720-2500
13 Facsimile: (858) 720-2555

14 R. WILLIAM BOWEN, JR. (102178)
15 GEN-PROBE INCORPORATED
16 10210 Genetic Center Drive
17 San Diego, California 92121-4362
18 Telephone: (858) 410-8918
19 Facsimile: (858) 410-8637

20 Attorneys for Plaintiff
21 Gen-Probe Incorporated

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23
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UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF CALIFORNIA

29 GEN-PROBE INCORPORATED,

30 No. 99-CV-2668H AJB
31 JUDGE MARILYN L. HUFF

32 Plaintiff,

33 REPLY DECLARATION OF DR. JOSEPH O.
34 FALKINHAM IN SUPPORT OF GEN-PROBE'S
35 MOTION FOR PARTIAL SUMMARY JUDGMENT

36 v.

37 Date: June 8, 2001
38 Time: 10:30 a.m.
39 Dept.: Courtroom 1

40 VYSIS, INC.,

41 Defendant.

J. Joseph O. Falkingham, III, hereby declare as follows:

1. I have personal knowledge of the facts set forth below, and, if called as a witness in this action, I could and would testify competently to the truth thereof.

2. I have been retained as an expert witness in this lawsuit. I have reviewed the specification and claims of the '338 patent), as well as Vysis, Inc.'s Opposition to Gen-Probe's Motion for Summary Judgment and the Declaration of Dr. David H. Persing. I submit this declaration to rebut certain statements made by Dr. Persing.

SUMMARY OF OPINION

3. In paragraph 13 of his declaration, Dr. Persing states that he believes that Example 5 describes specific amplification because:

"In particular, while Example 5 states initially that random oligohexamer primers can be used to achieve non-specific amplification, Example 5 also discloses that "[a]lternatively, the double stranded DNA can be formed by synthesis starting from capture probe a." Col. 31, lines 48-49. In this instance, the capture probe acts as the primer. Since the capture probe binds specifically to the target DNA, the capture probe would be a specific primer to the target. This is an example of specific amplification because the primer, capture probe a, binds to a specific, unique DNA sequence in the target organism."

4 I disagree with Dr. Persing's conclusion for the following reasons.

5. Example 5 of the '338 specification teaches only the combination of target capture with *non-specific* amplification. Example 5 is set forth in three paragraphs of text beginning at col. 31, line 24 of the '338 patent. The first paragraph consists of a single sentence that states that the example teaches non-specific amplification:

In this example, both *non-specific* replication of target DNA and transcription of that DNA are used to amplify capture target DNA.

(Exh. 8, at col. 31, ll. 24-54, emphasis added.) The second paragraph of example 5 provides the details of a particular method, and teaches the use of *random* (e.g., non-specific) primers and non-specific transcription in the amplification process used in the method. (Exh. 8, at col. 31, ll. 31-33.) As a result of these explicit statements, it is my opinion that a person skilled in the art would understand that Example 5 discloses a non-specific method of amplification.

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1 6. This understanding is reinforced by the fact that Example 5 refers to and
2 incorporates Figure 5 of the drawings included in the patent. (Exhibit 8 at col. 31, l. 28.) The
3 drawings, including Figure 5, are discussed and described in the text of the patent specification:

4 In Step 3 of FIGS. 4, 5 and 6, the isolated target is *non-specifically*
5 amplified to form a multitude of amplification products.

6 (Id. at col. 15, ll. 56-58, emphasis added.) Thus, Dr. Persing's contention that Example 5 teaches
7 specific amplification is contrary to the description of the Figure associated with Example 5.

8 7. Further, use of the capture probe as a primer in Example 5 of the '338 Patent does
9 not disclose amplification with specific primers. The addition of DNA polymerase and
10 nucleoside-triphosphates would simply result in the extension of the capture probe DNA molecule
11 by synthesis of a complement to the sequence of the target DNA not hydrogen-bonded to the
12 capture probe. This extension would occur only once. Extension of the capture probe is not
13 amplification of the target sequence. Because only a complement of the target would be
14 synthesized, there is no amplification of the target sequence. It is also not clear from Example 5
15 that even extension of the capture probe using the target DNA as template would occur. If the
16 capture probe was bound to the matrix through the 3' terminus such that its 5' end was free, there
17 could be no extension. DNA polymerases require a '3-OH end to initiate extension.

18 8. One of ordinary skill would recognize that the nucleic acid extension in Example 5
19 would not be amplification, which is exponential and involves repeated steps. Using the target
20 DNA as template would result in a one time, linear extension of the capture probe. The absence of
21 a second specific probe means that there would be no amplification or further replication of the
22 double-stranded DNA resulting from the DNA polymerase-catalyzed extension of the capture
23 probe.

24 9. Dr. Persing's conclusion that Example 5 discloses specific amplification is incorrect
25 because it is based on the incorrect assumption that the capture probe described in Example 5
26 "binds specifically to the target DNA." There is nothing in the 338 'patent that describes this
27 capture probe as one that "binds specifically to the target DNA." Rather, Example 5 says that
28 "denatured sample DNA is captured as described above". "Above" is Example 4, which simply

1 states that "A recA protein coated capture probe is then added to the digested target DNA . . . The
2 recA protein coated probe contains a nucleic acid sequence (a) that is homologous to a first target
3 (a') sequence of the target DNA, as well as a homopolymer sequence on a capture bead." These
4 passages do not state that the capture probe is specific to the target DNA. The fact that a probe is
5 "homologous" does not mean that the probe is specific. "Homologous" has a very specific
6 meaning in the art. Two sequences are "homologous" if one evolved from the other.

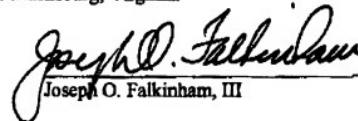
7 "Homologous" does not mean that the two sequences are complementary over their entire lengths.

8 10. Even if the '338 specification contained a description of a specific capture probe
9 which could be used as a primer (which it does not), then the result, as in paragraph 7, would be
10 extension, not amplification. Further, even a very specific capture probe would likely function
11 non-specifically as a primer under the very different reaction conditions of the processes of capture
12 and extension. For example, the conditions necessary for extension would promote non-specific
13 binding of the capture probe with the target DNA. Thus, the extension would be non-specific.

14 11. I have read Dr. Persing's comments regarding the prosecution history. These
15 comments do not change any of the opinions that I expressed in my original report or in this report.

16 I hereby declare under penalty of perjury under the laws of the United States of America
17 and the State of California that all statements made herein of my own knowledge are true and that
18 all statements made on information and belief are believed to be true. As discovery in this case is
19 now just beginning, I reserve the right to change or supplement my opinion. This declaration was
20 executed by me on this 1st day of June, 2001 at Blacksburg, Virginia.

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Joseph O. Falkingham, III

1 STEPHEN P. SWINTON (106398)
2 J. CHRISTOPHER JACZKO (149317)
COOLEY GODWARD LLP
3 4365 Executive Drive, Suite 1100
San Diego, CA 92121-2128
Telephone: (858) 550-6000
4 Facsimile: (858) 453-3555

5 DOUGLAS E. OLSON (38649)
BROBECK PHLEGER & HARRISON LLP
6 12390 El Camino Real
San Diego, CA 92130
7 Telephone: (858) 720-2500
Facsimile: (858) 720-2555

8 R. WILLIAM BOWEN, JR. (102178)
9 GEN-PROBE INCORPORATED
10 10210 Genetic Center Drive
San Diego, CA 92121-4362
Telephone: (858) 410-8918
11 Facsimile: (858) 410-8637

12 Attorneys for Plaintiff
GEN-PROBE INCORPORATED

13

14 UNITED STATES DISTRICT COURT
15 SOUTHERN DISTRICT OF CALIFORNIA

16

17 GEN-PROBE INCORPORATED,

18 Plaintiff,

19 v.

20 VYSIS, INC.,

21 Defendant.

22

No. 99CV2668 H (AJB)
THE HONORABLE MARILYN L. HUFF

23

REPLY DECLARATION OF CHRISTINE
GRITZMACHER IN SUPPORT OF GEN-PROBE'S
MOTION FOR PARTIAL SUMMARY JUDGMENT

24 Date: June 8, 2001
Time: 10:30 a.m.
Dept.: Courtroom 1

25 I, Christine Gritzmacher, declare as follows:

26 1. I am a member of the State Bar of California and admitted to practice before the
United States Patent and Trademark Office.

27 2. I am employed as Patent Counsel by Gen-Probe Incorporated and I make this
declaration in support of Gen-Probe's Motion for Partial Summary Judgment.

28 ///

1 3. Gen-Probe has obtained copies of the files of the United States Patent and
2 Trademark Office concerning United States Patent No. 5,750,338 and United States Patent No.
3 5,714,380.

4 4. I reviewed the files referred to in paragraph 3. This declaration is based on that
5 review. This declaration is prepared and offered pursuant to Rule 1006 of the Federal Rules of
6 Evidence. The complete patent prosecution files are voluminous and cannot conveniently be
7 examined in court in connection with Gen-Probe's Motion for Summary Judgment. I believe that
8 copies of the individual patent documents referred to in this declaration have been previously
9 submitted by the parties or are submitted as exhibits to accompanying reply notice of lodgment.

10 5. Vysis' first patent application claiming the combination of target capture and
11 amplification was filed on December 21, 1987. (Vysis Exhibit A.) The claims of this application
12 were rejected by Examiner Chambers. (Vysis Exhibit B.)

13 6. Vysis filed a "continuation" patent application on January 22, 1991 and the claims
14 of that second application were also rejected by Examiner Chambers. (Vysis Exhibit C.)

15 7. Vysis filed yet another continuation application on September 14, 1992, leading to a
16 third rejection by the same examiner in November 1992. (Vysis Exhibit D.) Because Vysis did
17 not respond to the November 1992 rejection, the third patent application was abandoned as of
18 February 5, 1993. (Exhibit 19 to Gen-Probe's Reply Notice of Lodgment.)

19 8. Vysis did not take any further steps to seek a patent for the invention of U.S. patent
20 number 5,750,338 until May 3, 1994, more than one year after it abandoned its third application.
21 In May 1994, Vysis petitioned the PTO to "revive" its third patent application. (Exhibit 20 to
22 Gen-Probe's Reply Notice of Lodgment.) That petition was denied by the PTO on the ground
23 Vysis had waited more than one year after abandonment to seek revival. (Exhibit 21 to Gen-
24 Probe's Reply Notice of Lodgment.)

25 9. In May 1994, Vysis filed a *fourth* application, an identical copy of the three prior
26 applications. While the prior three applications had all been assigned to the same patent examiner,
27 the fourth application was assigned to a different examiner. On December 5, 1995, in prosecution
28 of this fourth application, Vysis first suggested that the application encompassed methods of

specific amplification such as PCR. (Vysis Exhibit E.) That is, Vysis made this statement almost 8 years after the first patent application was filed.

3 10. Exhibit 22 to Gen-Probe's Reply Notice of Lodgment is a summary of the
4 prosecution history of the '338 patent. I believe Exhibit 22 is an accurate summary of the
5 information presented therein with respect to the prosecution history. This summary is prepared
6 and offered pursuant to Rule 1006 of the Federal Rules of Evidence.

7 11. As used in this declaration, the term "Vysis" is used to refer collectively to the
8 current patent owner, defendant Vysis, Inc., and to all of its predecessors in interest. The term
9 "Vysis" includes Vysis' parent and predecessor in interest, BP Amoco Corporation.

10 I declare under penalty of perjury under the laws of the United States of America that the
11 foregoing is true and correct.

Executed at San Diego, California on June 1, 2000.

Christine Gritzmacher
Christine Gritzmacher